REMARKS/ARGUMENTS

Claims 1, 2, 8-12, 15-20, 26-30, 33-38, 44-47, and 49-53 remain in the application. Claims 1, 19, and 53 has been amended. No claims have been canceled. Reconsideration of this application, as amended, is respectfully requested.

Claims 1 and 19 have been amended to supply a missing antecedent basis for a term.

Claim 53 has been amended to specify that the distance between (a) the source of light for irradiating a region of said biological sample with light and (b) the means for collecting light re-emitted from said region of said biological sample ranges from 0.44 millimeter to 1.84 millimeters. Support for this amendment can be found at page 33, line 22 through page 34, line 3 of the specification.

Claim 53 was rejected under 35 U. S. C. § 112, first paragraph, as failing to comply with the written description requirement. This rejection is respectfully traversed for the following reasons.

Claim 53 has been amended to conform to the disclosure in the specification. Accordingly, this rejection should be withdrawn.

Claims 1-2, 8-12, 15-20, 26-30, 33-38, 44-47, and 49-51 were rejected under 35 U. S. C. § 103 (a) as being unpatentable over U. S. Patent No. 5,978,691 to Mills in view of the journal publication "Effect of temperature on the optical properties of ex vivo human dermis and subdermis" by Laufer et al. in view of U. S. Patent No. 5,497,769 to Gratton et al. This rejection is respectfully traversed for the following reasons.

Mills, U. S. Patent No. 5,978,691 (hereinafter "Mills"), discloses a method for facilitating the noninvasive determination of characteristics of subject matter and the environment in which said subject matter exists, the method comprising the steps of:

Emitting at least one wavelength of electromagnetic radiation applied to said subject matter

Detecting said wavelength after contact with said subject matter

Inducing a temperature change in said subject matter while emitting and detecting said radiation applied to said subject matter

Computing parameters based on information processed from the contact of said radiation at various temperature levels on said subject matter.

Laufer et al., "Effect of temperature on the optical properties of ex vivo human dermis and subdermis" (hereinafter "Laufer et al."), discloses the effect of temperature on the optical properties of human dermis and subdermis as a function of near-infrared wavelength between 25 °C and 40 °C. Measurements were performed *ex vivo* on a total of nine skin samples taken from the abdomen of three individuals. Laufer et al. utilizes diffuse reflectance and transmission measurements carried out on thin dermis and subdermis samples at four different temperatures by means of an integrating sphere, which was placed in a temperature controlled environment. See page 2479 of Laufer et al.

Gratton et al., U. S. Patent No. 5,497,769 (hereinafter "Gratton et al."), discloses the quantitative determination of various materials in highly scattering media such as living tissue in an external, photometric manner by the use of a plurality of light sources positioned at differing distances from a sensor. The light from the sources is amplitude modulated, and, in accordance with conventional frequency domain fluorometry or phosphorimetry techniques, the gain of the sensor is modulated at a frequency different from the frequency of the light modulation. Data may be acquired from each of the light sources at differing distances at a frequency which is the difference between the two frequencies described above. From these sets of data from each individual light source, curves may be constructed, and the slopes used to quantitatively determine the amount of certain materials present, for example oxyhemoglobin and deoxyhemoglobin in living tissue.

All of the claims of this application require spatially resolved diffuse reflectance measurements of a biological sample. All of the claims of this application require that the biological sample comprise intact human tissue. See independent claims 1, 19, and 37, and the claims depending from

independent claims 1, 19, and 37, especially part (b) of claim 1, part (b) of claim 19, and part (d) of claim 37 for spatially resolved diffuse reflectance measurements, and part (g) of claim 1, part (g) of claim 19, and part (e) of claim 37 for the requirement of intact human tissue. Mills fails to disclose spatially resolved diffuse reflectance measurements of a biological sample. Laufer et al. fails to disclose spatially resolved diffuse reflectance measurements of a biological sample. Gratton et al. fails to disclose spatially resolved diffuse reflectance measurements of a biological sample. Spatially resolved diffuse reflectance measurements are described in detail at page 21, line 14 through page 22, line 3, and at page 31, line 9 through page 45, line 28 of the specification. Gratton et al. discloses the use of the same method of detection and circuitry as is used in frequency domain fluorometry and/or phosphorimetry, which are distinguishable from spatially resolved diffuse reflectometry. See column 4, lines 35-41 and column 6, lines 45-55 of Gratton et al. For the foregoing reasons, it is submitted that the combination of Mills et al, Laufer et al., and Gratton et al. fails to render claims 1-2, 8-12, 15-20, 26-30, 33-38, 44-47, and 49-51 obvious to one of ordinary skill in the art.

It is clear that both Mills et al. and Gratton et al. disclose non-invasive processes that make use of a biological sample that comprises intact human tissue. However, it is also clear that Laufer et al. does not and cannot make use of a biological sample that comprises intact human tissue. According to Laufer et al., at page 2481, lines 8-9, of section *2.3. Measurement methods*:

> ".....Illumination of both sides of the sample was necessary as the samples of the dermis have different reflectivities from opposite sides....." (emphasis added)

According to Laufer et al. at page 2482, line 1 of section **3. Results**:

> "The optical coefficients were calculated for the front and back illumination of each sample....." (emphasis added)

According to these statements, there can be no doubt that the method of Laufer et al. is an invasive method that cannot be practiced on a biological sample comprising intact human tissue. According to Laufer et al., in order to measure the optical properties of the subdermis or deeper layers of the tissue, one must illuminate both sides of the sample, i.e., the front side and the back side. In order to carry out this manner of illumination, the tissue must be excised from the human subject, and, consequently, the tissue **cannot** be intact human tissue. Breaching intact human tissue would completely defeat the purpose of the present invention, which is to measure optical parameters of a biological sample non-invasively. Thus, the combination of Laufer et al., which requires breaching of human tissue, with Mills et al. and Gratton et al., which require intact human tissue, is impermissible. In effect, the combination of Mills et al, Laufer et al., and Gratton et al. is based on a piecemeal reconstruction of the prior art. It is impermissible within the framework of 35 U. S. C. § 103 to pick and choose from any one reference (i.e., Laufer et al.) only so much of it as will support a given position (i.e., effect of temperature on the scattering coefficient), to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art (i.e., measurement of scattering coefficient with excised human tissue, that is, human tissue that is not intact). For this reason, too, it is submitted that the combination of Mills et al, Laufer et al., and Gratton et al. fails to render claims 1-2, 8-12, 15-20, 26-30, 33-38, 44-47, and 49-51 obvious to one of ordinary skill in the art.

Claim 52 was rejected under 35 U. S. C. § 103 (a) as being unpatentable over U. S. Patent No. 5,978,691 to Mills in view of the journal publication "Effect of temperature on the optical properties of ex vivo human dermis and subdermis" by Laufer et al. in view of U. S. Patent No. 5,497,769 to Gratton et al., and further in view of U. S. Patent No. 5,873,821 to Chance et al. This rejection is respectfully traversed for the following reasons.

Chance et al., U. S. Patent No. 5,873,821 (hereinafter "Chance et al. '821"), discloses an oximeter disposed on an endoscope, catheter or guidewire or the like for insertion via a body passage to internal tissue, and including means such as an inflatable balloon to press the oximeter sensor against the localized tissue of interest.

Claim 37 requires that the biological sample comprises intact human tissue. For the same reasons that claims 1-2, 8-12, 15-20, 26-30, 33-38, 44-47, and 49-51 are not obvious to one of ordinary skill in the art, claim 52 is not obvious to one of ordinary skill in the art.

Claims 1, 8, 9-12, 15-16, 19, 26-28, 29-30, 33-34, 37-38, 44-47, 49 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13, 40, and 42-43 of U. S. Patent No. 6,662,030 to Khalil et al. in view of the journal publication "Effect of temperature on the optical properties of ex vivo human dermis and subdermis" by Laufer et al., and further in view of U. S. patent No. 5,497,769 to Gratton et al. This rejection respectfully traversed for the following reasons. This rejection is respectfully traversed for the following reasons.

A Terminal Disclaimer is being submitted herewith to remove U. S. Patent No. 6,662,030 to Khalil et al. as a reference. For this reason, this rejection can be withdrawn.

In view of the foregoing, it is submitted that claims 1, 2, 8-12, 15-18, 19, 20, 26-30, 33-36, 37, 38, 44-47, and 49-53 are in condition for allowance, and official Notice of Allowance is respectfully requested.

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Respectfully submitted,
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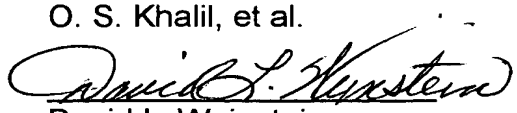

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